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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/387,340	08/31/99	NEEDLEMAN P	MON-102.0-CO

EXAMINER	
DAVIS,M	
ART UNIT	PAPER NUMBER
1642	7

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/387,340	Applicant(s) Needleman et al
	Examiner Minh-Tam Davis	Group Art Unit 1642

☒ Responsive to communication(s) filed on *Jul 12, 2000*.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *11, 12, 14, and 15* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *11, 12, 14, and 15* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Minh-Tam Davis, Group Art Unit 1642.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Accordingly, claims 11, 12, 14, 15 are being examined.

The following are the remaining rejections.

DOUBLE PATENTING

Rejection under 35 USC 101 of claims 11, 12 pertaining to obviousness double patenting over claims 1-11, 15-16, 22-27 of the copending application, SN=08/93437 remains for reasons already of record in paper No.5.

Applicant argues that the copending application, SN=08/93437 has not yet indicated to be allowable, and therefore, this issue of double patenting is not ripe as to this application.

This rejection remains because the issue of double patenting is independent of whether the applications are allowable or not. Further, it is noted that the rejection is made provisionally because the conflicting claims have not been patented.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH

Rejection under 35 USC 112, first paragraph of claims 11, 12, 14, 15 pertaining to lack of enablement for a method of increasing the concentration of HDL cholesterol remains for reasons already of record in paper No. 5.

Applicant argues as follows:

The disclosures of the application, including the p values, show that it is more likely than not that the CETP immunogens raised the HDL value compared to the control immunogen. Whether one would desire a greater significance and smaller p value for publication in a referred journal or for submission to the FDA is not relevant here. Rather, what is relevant is whether a person of ordinary skill in the art would see the disclosures as a whole as a reasonable evidentiary showing that the immunization was successful.

Applicant's arguments set forth in paper No.6 have been considered but are not deemed to be persuasive for the following reasons:

The Examiner agrees that the issue here is not a desire of a greater significance and smaller p value for publication in a referred journal or for submission to the FDA. The issue here is that because the disclosed p value of 0.17 in table 1 (p.40) is not at a significant level ($p<=0.05$), and therefore the 10% difference disclosed in table 1 could be due to variation within sample, rather than to a significance difference in HDL levels between the control and the animals immunized with recombinant human CETP, or with rabbit CETP C-terminal having 26 amino acids in length conjugated to thyroglobulin. In other words, the difference in HDL levels seen in table 1 could be the noise level due to variation within samples, and there would not be any

DETAILED ACTION

Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Minh-Tam Davis, Group Art Unit 1642.

Election/Restriction

1. Restriction to one of the following species is required under 35 U.S.C. 121:

   I. Claims 11-13, drawn to drawn to a process for increasing the concentration of HDL in the blood of a mammal, comprising immunizing said mammal with a fusion protein, wherein said fusion protein comprises a carrier peptide-bonded to the carboxy or amino terminus of CETP, classified in class 514, subclass 2.

   II. Claims 11, 12, 14, 15, drawn to a process for increasing the concentration of HDL in the blood of a mammal, comprising immunizing said mammal with a fusion protein, wherein said fusion protein comprises a carrier peptide-bonded to both the carboxy and amino termini of CETP, wherein the construct is as in claim 14(a), classified in class 514, subclass 2.

   III. Claims 11, 12, 14, 15, drawn to a process for increasing the concentration of HDL in the blood of a mammal, comprising immunizing said mammal with a fusion protein, wherein said fusion protein comprises a carrier peptide-bonded to both the

carboxy and amino termini of CETP, wherein the construct is as in claim 14(b), classified in class 514, subclass 2.

IV. Claims 11, 12, 16, 17, drawn to a process for increasing the concentration of HDL in the blood of a mammal, comprising immunizing said mammal with a fusion protein, wherein said fusion protein comprises a carrier peptide-bonded to both the carboxy and amino termini of CETP, wherein the construct is as in claim 16, classified in class 514, subclass 2.

2. The inventions are distinct, each from the other because of the following reasons:

The methods of species I-IV are distinct, because they use different constructs, using different seqeunces of Hepatitis core protein, wherein not all amino acid sequences from Hepatitis core protein are immunogenic, and wherein amino- or carboxy-terminal linkage to CEPT would produce different immunogenic properties as compared to linkage to both amino and carboxy-termini of CETP.

Because these inventions are distinct for the reason given above and have acquired a separate status in the art, and because the searches for the groups are not co-extensive, restriction for examination purposes as indicated is proper.

A telephone call was made to Edward Gamson on 01/03/2000, to request an oral election to the above restriction requirement, and resulted in an election with traverse to prosecute the invention of species III, claims 11, 12, 14, 15.

Accordingly, claims 11, 12, 14, 15, immunizing with construct of claim 14(b), are examined in this application. Affirmation of this election must be made by applicant in responding to this Office action.

REJECTION UNDER 35 USC 101, DOUBLE PATENTING

35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Double patenting rejection of copending applications Serial Nos: 08/785997, and 08/788,882 are not determined at this time, because said cases are not available.

Claims 11 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11, 15-16, 22-27 of copending application Serial No. 08/ 934367. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims 11, and 12 in the present application are drawn to immunizing a mammal with a fusion protein, wherein said fusion protein comprises an exogeneous antigenic carrier polypeptide that is peptide-bonded to both the amino- and carboxy-termini of cholesteryl ester transfer protein (CETP), whereas the claims 1-11, 15-16, 22-27 are drawn to immunizing a mammal with a DNA molecule encoding a fusion protein, wherein said fusion protein comprises an exogeneous antigenic carrier polypeptide that is covalently bonded to a CETP sequence of about 10 to about 30 amino acids.

The claims 11 and 12 of the instant application, and the claims 1-11, 15-16, 22-27 of the application Serial No. 08/ 934367 are thus obvious variants.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Therefore, the inventions as claimed are co-extensive.

REJECTION UNDER 35 USC 112, SECOND PARAGRAPH

Claims 11, 12, 14, 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 11 is indefinite for the use of the language "lesson". It seems that applicant mispells the word "lessen".

2. Claim 11 is indefinite for the use of the language "about 10 percent or more", which does not set forth the metes and bounds of the patent protection desired.

3. The term "essentially" in claim 14 is a relative term which renders the claim indefinite. The term "essentially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

4. Claim 14 is indefinite for the use of the language " position 10 about position 183". It seems that applicant inadvertently omits the word "to", and intends to claim " position 10 to about position 183".

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, ENABLEMENT

Claims 11, 12, 14, 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled

in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 11, 12, 14, 15 are drawn to a process for increasing the concentration of high density lipoprotein (HDL) cholesterol by about 10 percent or more in blood of a mammal, by immunizing with the immunogen cholesteryl ester transfer protein (CETP). The immunogen CETP was fused at both amino- and carboxy-termini, with an antigenic carrier, hepatitis B core protein (HBcAg). The following is the construct of the above immunogen CETP flanked by the amino- and carboxy- termini of HBcAg sequences: The immunogen CETP has a) a sequence of about 10 to about 30 amino acids in length, or b) the sequence of the CETP carboxy-terminal 30 amino acids, including the polypeptide of SEQ ID No:10. The amino-terminal flanking carrier HBcAg sequence consists essentially of about 70 to about 90 amino acids in length, and is from about amino acid position 1 to about amino acid position 90. The carboxy-terminal HBcAg sequence consists essentially of about 65 to about 85 amino acids in length, and is from about amino acid position 80 to about amino acid position 183.

It is unpredictable that the claimed method would significantly increase the concentration of HDL, by immunizing with CETP conjugated to both amino- and carboxy-termini of an antigenic carrier, hepatitis B core protein (HBcAg). The specification dislcoses in table 1 that the p value for HDL level after injection of recombinant human CETP (rhCETP), or C-terminal 26 rabbit CETP amino acids conjugated to an antigenic carrier, thyroglobulin (CETP-TH) is 0.17 and 0.38, respectively, as c ompared to the control. It is well known in the art that a p value from a

Student's T test should be less or equal to 0.05 to significant. In other words, the 10 percent difference seen in table 1 is due to variation within samples, rather than to a significant difference in HDL between the control and the animals immunized with recombinant human CETP, or with C-terminal 26 rabbit CETP conjugated to thyroglobulin. One of skill in the art would not have expected that immunization with CETP conjugated to hepatitis B core protein would significantly increase the level of HDL, because immunization with a construct of CEPTconjugated to thyroglobulin, does not significantly increase the level of HDL, and because applicant does not disclose any working example wherein immunization with CETP conjugated to both amino- and carboxy-termini of hepatitis B core protein would significantly increase the level of HDL. In view of the above, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Minh-Tam B. Davis whose telephone number is (703) 305-2008. The examiner can normally be reached on Monday-Friday from 10:00 am to 2:00 pm, except on Wesnesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tony Caputa, can be reached on (703) 308-3995. The fax phone number for this Group is (703) 308-4227.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0916.

Minh-Tam B. Davis

March 17, 2000

SUSAN UNG
PATENT EXAMINER